General

Guideline Title

The insertion and management of external ventricular drains: an evidence-based consensus statement: a statement for healthcare professionals from the Neurocritical Care Society.

Bibliographic Source(s)

Fried HI, Nathan BR, Rowe AS, Zabramski JM, Andaluz N, Bhimraj A, Guanci MM, Seder DB, Singh JM. The insertion and management of external ventricular drains: an evidence-based consensus statement: a statement for healthcare professionals from the Neurocritical Care Society. Neurocrit Care. 2016 Feb;24(1):61-81. [153 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions of the strength of recommendations (*strong, conditional, good practice*) and quality of the evidence (*high, moderate, low, very low*) are provided at the end of the "Major Recommendations" field.

Is There an Increased Risk of Adverse Mechanical or Infectious Events in Adult Patients Undergoing External Ventricular Drain (EVD) Insertion Outside the Operating Room?

See Evidentiary Table 1 (see the "Availability of Companion Documents" field for all evidentiary tables).

Recommendation

The Committee suggests that the location of EVD insertion (operating room [OR] or bedside) should be dictated by patient characteristics and clinical circumstances. (*Conditional recommendation; low-quality evidence*)

In making this recommendation, the Committee acknowledges that there is a lack of conclusive evidence demonstrating equivalence of EVD insertion within and outside the OR, but the available data suggest that EVD insertion outside the OR is associated with a sufficiently low rate of complications that it is an acceptable option depending on the clinical situation and OR availability. A standardized protocol can minimize risks of complications regardless of where the procedure is performed. The importance of evidence-based protocol for the insertion and management of EVDs is covered later in these guidelines.

In Adult Patients Undergoing EVD Insertion, Does the Risk of Adverse Events Vary Depending on the Training, Procedural Experience, or

Specialty of the Clinician Performing the Procedure?

See Evidentiary Table 2.

Good Practice Statement

The Committee suggests that practitioners planning to place EVDs follow formal institutional protocols for training, mentoring, and quality assurance. The Committee suggests that neurosurgeons participate in development of the institutional protocol and credentialing, and that neurosurgical backup availability be assured.

The Committee found no evidence that type of training, experience, or specialty affect the risk of complications during EVD insertion.

What Is the Risk of Hemorrhage with EVD Insertion? Are There Modifiable Factors That Can Reduce This Risk?

See Evidentiary Table 3.

Good Practice Statement

Except in dire emergencies requiring immediate ventricular decompression, coagulopathy should be corrected according to institutional protocols before insertion of an EVD.

The Committee determined that no adequately powered and ethical study is likely to be performed comparing reversal of antithrombotic or anticoagulant drugs prior to the insertion of EVD. However, they felt unanimously that given the potentially devastating effect of even a small hemorrhage, taking all measures possible to minimize hemorrhagic complications is in keeping with good clinical practices.

What Procedural Factors Are Associated with a Decreased Risk of Catheter Malposition?

See Evidentiary Table 4.

Recommendation

When ventricular anatomy is normal, the Committee suggests using Kocher's point as entry, and a trajectory perpendicular to the skull or targeting the contralateral medial canthus to provide the highest likelihood of optimal EVD placement. The catheter should not be advanced more than 6.5 cm from the skull surface before cerebrospinal fluid (CSF) is encountered.

In cases of distorted ventricular anatomy or unusually small ventricles, consider using image guidance if available.

Observational clinical series and computer simulations show that the above landmarks provide the highest rates of successful placement in the frontal horn.

(*Conditional recommendation; low-quality evidence*)

In Adult Patients Requiring EVD, What Is the Optimal Method and Timing of Venous Thromboembolism (VTE) Prophylaxis?

See Evidentiary Table 5.

Recommendations

In adult patients with an EVD:

- The Committee recommends VTE prophylaxis for the duration of immobilization. (*Strong recommendation; low-quality evidence*)
  In making this recommendation, the Committee considered both the high incidence of VTE and the evidence supporting the efficacy of prophylaxis at preventing VTE in patients similar to the population in question.
- The Committee recommends against the routine use of inferior vena cava (IVC) filters for primary prophylaxis of VTE. (*Strong recommendation; low-quality evidence*)
  In making this recommendation, the Committee considered the evidence suggesting possible harm and the paucity of data supporting the efficacy of IVC filters for VTE prophylaxis.
- The Committee recommends the use of mechanical VTE prophylaxis (sequential compression device or intermittent pneumatic compression) in all patients with contraindications to pharmacological prophylaxis (unfractionated heparin [UFH] or low-molecular-weight heparin [LMWH]) and without contraindications to mechanical devices. (*Conditional recommendation; low-quality evidence*)
- In patients with additional risk factors for VTE (including, but not limited to concurrent malignancy, trauma, spinal cord injury, critical illness,

and immobilization), we suggest pharmacological prophylaxis after an intracranial hemorrhage has been ruled out or is stable. (*Conditional recommendation; low-quality evidence*)
In making these recommendations, the Committee weighed the individualized risk of VTE, the strength of evidence showing incremental efficacy of pharmacoprophylaxis over mechanical prophylaxis, and the increased risk of major hemorrhage associated with pharmacological prophylaxis.

In Adult Patients with an EVD, Does the Risk of Infection Increase with Duration of Placement?

See Evidentiary Table 7.

Good Practice Statement

External ventricular drains should be removed as early as the clinical situation allows.

In making this statement, the Committee determined that there is sufficient evidence of ongoing risk of ventriculostomy-related infection (VRI) to mandate removal of the EVD as soon as it is no longer indicated.

In Adult Patients, Do Prophylactic Systemic Antimicrobials Reduce the Incidence of VRI? Should a Periprocedural or Duration Regimen Be Used?

See Evidentiary Table 8.

Recommendations

- The Committee suggests one dose of antimicrobials prior to EVD insertion. (*Conditional recommendation; low-quality evidence*)
- The Committee recommends against the use of antimicrobials for the duration of EVD placement; duration regimens may increase the risk of resistant organisms and *Clostridium difficile* colitis. (*Strong recommendation; low-quality evidence*)

The Committee made this strong recommendation based on the potential for harm related to C. difficile *diarrhea and antimicrobial-resistant organisms, as well as the lack of demonstrated efficacy of duration regimen antimicrobials*.

Good Practice Statement

There is insufficient evidence to recommend a specific antimicrobial to be used in periprocedural prophylaxis. The Committee recommends the use of local antibiograms to guide periprocedural antimicrobial selection.

In Adult Patients with an EVD, Does the Use of Antimicrobial-Impregnated Catheters Reduce the Incidence of VRI?

See Evidentiary Table 9.

Recommendation

The Committee recommends using antimicrobial-impregnated catheters as part of a comprehensive management protocol to reduce the rate of VRI. (*Strong recommendation; moderate-quality evidence*)

In making this recommendation, the Committee felt that overwhelming evidence, though most of it retrospective, supports the use of antimicrobial-impregnated catheters as part of a regimen to reduce VRI. Additionally, the benefit:risk ratio is positive. There is insufficient evidence to compare the efficacy of antibiotic-impregnated and silver-impregnated catheters. Individual institutions and practitioners should choose catheters based on availability and cost.

Are Additional Intraventricular Antimicrobials Effective for the Treatment of VRI as Compared to Intravenous Antimicrobials Alone?

See Evidentiary Table 10.

Recommendation

The Committee recommends using intraventricular antimicrobials to treat ventriculostomy-related infections in patients who fail to respond to intravenous antimicrobials alone or when organisms have high minimum inhibitory concentrations (MICs) to antimicrobials that do not achieve high CSF concentrations, especially multidrug-resistant organisms. Strong consideration should be given to involving an infectious diseases expert in making this decision and choosing the appropriate antimicrobials. (*Strong recommendation; moderate-quality evidence*)

In making this recommendation, the Committee determined that in cases where a VRI has not responded to intravenous antimicrobials,

the therapeutic alternatives are limited. Since the existing data support their safety and efficacy, the use of intraventricular antimicrobials is reasonable in this situation.

In Adult Patients Requiring an EVD, Does Routine CSF Sampling Increase EVD-Related Infections as Compared to Maintaining a Closed System with Sampling of CSF Only When Clinically Indicated?

See Evidentiary Table 11.

Recommendation

The Committee suggests avoiding routine CSF sampling and obtaining CSF for analysis only when clinically indicated. (*Conditional recommendation; low-quality evidence*)

The Committee recognized that there is significant uncertainty about the best estimates of benefits and harms related to the frequency of CSF sampling and that depending on local circumstances, other alternatives may be equally reasonable.

In Adult Patients Requiring an EVD, Do Routine Catheter Changes Decrease the Incidence of VRI Compared to No Catheter Changes?

See Evidentiary Table 12.

The Committee recommends against routinely changing catheter sites (*Strong recommendation; moderate-quality evidence*).

In issuing this recommendation, the Committee considered the lack of evidence supporting routine catheter changes along with the demonstrated risk of VRI associated with catheter changes.

In Adult Patients Requiring an EVD, Does Gradual Weaning Decrease the Incidence of Hydrocephalus and Need for Ventriculoperitoneal (VP) Shunting as Compared to Immediate Clamping?

See Evidentiary Table 13.

Good Practice Statement

EVD weaning should be accomplished as quickly as is clinically feasible so as to minimize the total duration of EVD monitoring and VRI risk.

In making this statement, the Committee prioritized the early discontinuation of EVD and the resultant reduction in EVD-associated VRIs even though there is one small trial supporting the equivalence of rapid and gradual EVD weaning strategies.

In Adult Patients Requiring an EVD, Does the Type of Dressing Reduce VRI?

See Evidentiary Table 14.

Good Practice Statement

Cleansing the insertion site using an antimicrobial agent at the time of EVD insertion and using a dressing as part of a management bundle is considered safe and effective practice.

The lack of studies evaluating the effect of various dressing choices on VRI rates limited the Committee's ability to evaluate this issue.

In Adult Patients, Does Routinely Changing the Tubing and Collection Devices Decrease the Incidence of EVD-Related Infection?

See Evidentiary Table 15.

Good Practice Statement

The EVD collection system should be manipulated as little as possible.

In making this statement, the Committee prioritized the prevention of VRIs. Although there are no high- or moderate-quality studies to guide decision making, the existing data suggest only potential harm from routine manipulation and no studies suggest benefit.

In Adult Patients, Does Introduction of an EVD Management Bundle Reduce the Risk of EVD-related Infections?

See Evidentiary Table 16.

Recommendation

The Committee recommends using an EVD management bundle that includes aseptic insertion, limits manipulation of the closed system, and standardizes dressings and weaning to reduce VRI. (*Strong recommendation; moderate-quality evidence*)

In making this recommendation, the Committee recognized the benefit of a bundled approach to prevent VRI but could not determine which individual components would be most impactful due to the variability in study methodology.

Definitions

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Criteria for Quality of Evidence

Quality of Evidence	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Strength of Recommendation

Strength of Recommendation	Description
Strong	Most patients should receive the intervention.
Conditional	Most patients would benefit from the intervention, though some may not. The pros and cons of the intervention should be assessed taking into account the available evidence and the values and preferences of the patient.
Good Practice	There is a high confidence in the estimates of the effect of the intervention, but there is only indirect evidence that would be challenging to subject to a formalized Grading of Recommendations Assessment, Development and Evaluation (GRADE) evaluation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Conditions requiring placement of external ventricular drains (EVDs), (e.g., traumatic brain injury, elevated intracranial pressure, acute hydrocephalus, other intracranial pathologies)

Guideline Category

Management

Prevention

Risk Assessment

Clinical Specialty

Critical Care

Emergency Medicine

Internal Medicine

Neurological Surgery

Neurology

Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To develop a formal, multidisciplinary, evidence-based Consensus Statement* regarding external ventricular drains (EVD) insertion and management

*Consensus Statement is defined by the Neurocritical Care Society as "recommendations developed using available evidence and expert opinion in areas where high quality clinical data is limited or does not exist for controversial clinical dilemmas."

Target Population

Adult patients undergoing external ventricular drain (EVD) placement

Interventions and Practices Considered

1. Location of external ventricular drain (EVD) insertion based on patient characteristics and clinical circumstances
2. Creation and use of institutional protocols
3. Coagulopathy before insertion
4. Consideration of drain insertion point and trajectory
5. Venous thromboembolism (VTE) prophylaxis
6. Removal of drains as soon as possible
7. Use of antimicrobials, including antimicrobial catheters
8. Cerebral spinal fluid (CSF) sampling only when indicated
9. Use of EVD management bundle

Note: The following were considered but not recommended: routine CSF sampling, routine catheter changes.

Major Outcomes Considered

- Rate of adverse events
- Risk of adverse events (risk of bleeding, risk of catheter malposition, risk of infection)
- Incidence of ventriculostomy-related infection (VRI)
- Incidence of hydrocephalus

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The Committee generated a set of clinical questions relevant to external ventricular drain (EVD) insertion and management specifying the patient group of interest, the intervention, the comparators, and the outcomes of interest (PICO format).

With the assistance of a medical librarian, the Committee undertook a comprehensive literature search of the PubMed, EMBASE, and Cochrane databases from 1960 to October 2014. The full search strategy is provided in the supplementary materials (see the "Availability of Companion Documents" field). The Committee did not consider articles in languages other than English, case series of five or less, primarily pediatric studies, nonhuman studies, or unpublished presentations. Pediatric studies were excluded as the Committee lacked the expertise to critically evaluate the pediatric literature. Abstracts of each citation were reviewed by two Committee members for relevance, and full-text articles were obtained where applicable. The Committee considered systematic reviews and meta-analyses but did not use them in evidence tables. Also included for analysis were articles identified in bibliographies and personal files which included references up to April 2015. Two experts focused on each PICO question.

Results of the Search

The initial search returned the following results:

- Returned 2520 unique references in the Infection search
- Returned 2392 unique references in the Insertion Complications search
- Returned 1607 unique references in the Management search

Duplicates between the three search strategies were eliminated for a total of 3578 unique references.

Number of Source Documents

All references were reviewed by at least one Committee member. Initial review produced a list of *pertinent* papers (about 10% of total):

- A total of 529 *pertinent* references in the Infection search
- A total of 302 *pertinent* references in the Insertion Complications search
- A total of 68 *pertinent* references in the Management search

Subsequent review of each of the papers by a minimum of 2 Committee members, reduced the number of references by another 90%.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Criteria for Quality of Evidence

Quality of Evidence	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The Committee utilized Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology to adjudicate the quality of evidence as high, moderate, low, or very low based on their confidence that the estimate of effect was close to the true effect (see the "Rating Scheme for the Strength of the Evidence" field). They generated recommendations only after considering quality of evidence, relative risks and benefits, patient values and preferences, and resource allocation.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

A committee of experts in neurosurgery, neurology, neuroinfectious disease, neurocritical care, internal medicine, pharmacotherapy, and nursing was recruited from within the Neurocritical Care Society. An organizational meeting was held in Seattle in September 2014. The Committee generated a set of clinical questions relevant to external ventricular drain (EVD) insertion and management specifying the patient group of interest, the intervention, the comparators, and the outcomes of interest (PICO format).

The Committee generated recommendations after considering quality of evidence, relative risks and benefits, patient values and preferences, and resource allocation. Recommendations were made for or against an intervention, and classified as strong ("the Committee recommends") or conditional ("the Committee suggests") (see the "Rating Scheme for the Strength of the Recommendations" field). Strong recommendations are the preferred course of action for most patients and should be adopted as policy in most situations. Conditional recommendations require further consideration within the clinical and institutional context and should be carefully evaluated by stakeholders before being implemented as policy.

The Committee recognized from the outset that high-quality evidence in the field of neurocritical care is seldom available. There is also growing awareness that many guidelines make strong recommendations based on low or very low-quality evidence. In some cases, these "discordant" recommendations may be inconsistent with Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology, possibly undermining clinicians' confidence in implementing the guidelines. GRADE methodologists have attempted to distinguish between recommendations based on a formal GRADE process and those better described as "good practice statements." The latter are recommendations where there is a high level of certainty in net benefit (or harm), but where published evidence is lacking, or is high quality but indirect. The Committee identified several questions where a "good practice statement" appeared more appropriate and identified them as such. They strove to make explicit the rationale behind each recommendation, including the weighing of risks and benefits and the basis for their level of confidence in the evidence (see the "Major Recommendations" field).

A meeting of the full Committee was held on March 7–8, 2015 in Denver. Topic authors presented GRADE evidence summaries, and recommendations were arrived at after discussion by the entire panel. On July 24, 2015, the entire Committee participated in a conference call to approve the final document.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

Strength of Recommendation	Description
Strong	Most patients should receive the intervention.
Conditional	Most patients would benefit from the intervention, though some may not. The pros and cons of the intervention should be assessed taking into account the available evidence and the values and preferences of the patient.
Good Practice	There is a high confidence in the estimates of the effect of the intervention, but there is only indirect evidence that would be challenging to subject to a formalized Grading of Recommendations Assessment, Development and Evaluation (GRADE) evaluation.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The final Consensus Statement was submitted for review by experts within the Neurocritical Care Society and by reviewers from other stakeholder societies (American Association of Neurological Surgeons, Congress of Neurological Surgeons, Infectious Diseases Society of America and Society for Critical Care Medicine). Further edits were made after these reviews.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate insertion and use of external ventricular drains to prevent complications

Potential Harms

- The benefits of external ventricular drains (EVDs) can be offset by procedural and catheter-related complications, such as hemorrhage along the catheter tract, catheter malposition, and cerebrospinal fluid (CSF) infection.
- Almost all patients undergoing EVD placement are at moderate to high risk of perioperative venous thromboembolism (VTE). A retrospective study evaluating the timing of heparin prophylaxis after EVD placement reported a VTE incidence of 7.2%. Rates of proximal deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients undergoing neurosurgical procedures with either no VTE

prophylaxis or elastic stockings alone are reported between 14% and 16%, although other studies have reported rates as high as 33%. The risk of VTE is greater in patients with primary central nervous system (CNS) malignancies (7.5%) and metastatic disease (17%).

- The use of antithrombotic agents for VTE prophylaxis is associated with an increase in bleeding complications. A comprehensive review and guideline statement found that compared with no prophylaxis, both unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) thromboprophylaxis were associated with a significantly increased risk of nonfatal major bleeding, including intracranial hemorrhage (relative risk of nonfatal bleeding 1.57 [95% confidence interval (CI) 1.32–1.87] for UFH and 2.03 [95% CI 1.37–3.01] for LMWH compared to no prophylaxis).
- A systematic review noted numerous adverse outcomes associated with inferior vena cava (IVC) filter placement (DVT 9.3%, insertion site thrombosis 2.0%, IVC thrombosis/occlusion 1.6%, complications during insertion 1.4%, and filter migration 0.4%). Data suggest that IVC filters prevent pulmonary embolism (PE), but cause at least as many DVTs and are associated with other complications.
- The use of long duration antimicrobials can lead to growth of antimicrobial-resistant organisms and to an increased incidence of *Clostridium difficile* colitis.
- In one study, risk factors associated with ventriculostomy-related infection (VRI) included intraventricular hemorrhage ($p = 0.027$), irrigation ($p = 0.021$), and ventricular catheterization for more than 5 days ($p = 0.017$).

Qualifying Statements

Qualifying Statements

Qualifying Statements

The Committee recognized from the outset that high-quality evidence in the field of neurocritical care is seldom available. There is also growing awareness that many guidelines make strong recommendations based on low or very low-quality evidence. In some cases, these "discordant" recommendations may be inconsistent with Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology, possibly undermining clinicians' confidence in implementing the guidelines. GRADE methodologists have attempted to distinguish between recommendations based on a formal GRADE process and those better described as "good practice statements." The latter are recommendations where there is a high level of certainty in net benefit (or harm), but where published evidence is lacking, or is high quality but indirect.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Fried HI, Nathan BR, Rowe AS, Zabramski JM, Andaluz N, Bhimraj A, Guanci MM, Seder DB, Singh JM. The insertion and management of external ventricular drains: an evidence-based consensus statement: a statement for healthcare professionals from the Neurocritical Care Society. Neurocrit Care. 2016 Feb;24(1):61-81. [153 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb

Guideline Developer(s)

Neurocritical Care Society - Medical Specialty Society

Source(s) of Funding

Neurocritical Care Society

Guideline Committee

External Ventricular Drain Guideline Writing Committee

Composition of Group That Authored the Guideline

Committee Members: Herbert I. Fried, University of Colorado and Denver Health Medical Center, Denver, CO, USA; Barnett R. Nathan, University of Virginia, Charlottesville, VA, USA; A. Shaun Rowe, College of Pharmacy, University of Tennessee Health Science Center, Knoxville, TN, USA; Joseph M. Zabramski, Barrow Neurological Institute, Phoenix, AZ, USA, Scottsdale Osborn Medical Center, Scottsdale, AZ, USA; Norberto Andaluz, University of Cincinnati College of Medicine, University of Cincinnati Neuroscience Institute and Mayfield Clinic, Cincinnati, OH, USA; Adarsh Bhimraj, Cleveland Clinic, Cleveland, OH, USA; Mary McKenna Guanci, Massachusetts General Hospital, Boston, MA, USA; David B. Seder, Department of Critical Care Services, Maine Medical Center, Portland, ME, USA, Tufts University School of Medicine, Boston, MA, USA; Jeffrey M. Singh, Department of Medicine, University of Toronto and Krembil Neuroscience Centre, Toronto Western Hospital, Toronto, Canada

Financial Disclosures/Conflicts of Interest

The authors do not have any conflicts of interest to declare.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Neurocritical Care Web site .

Availability of Companion Documents

Supplementary material is available from the Neurocritical Care Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on November 8, 2016. The information was verified by the guideline developer on December 8, 2016.

Copyright Statement

Disclaimer

NGC Disclaimer